X

TYPHOID BACILLURIA.

R.DODS BROWN M.B., Ch. B.

I

Historical.

Close on a quarter of a century has passed since the condition of Typhoid Bacilluria was originally described, but although so many years have elapsed comparatively little attention has been paid to this highly important subject.

For long the stools have been looked on as the cause of the dissemination of typhoid or enteric fever to the almost entire neglect of the urine. In 1873 Dr. Budd said (in "Typhoid Fever, its Nature, "Mode of spread and Prevention") "all the emanations "from the sick are in a certain degree infectious. "But at the same time it is one of the principal ob- "jects of this work to show that what is cast off from "the intestine is incomparably more virulent than "anything else."

Mention of the presence of bacilli in the urine of patients suffering from enteric fever appears to have been made first of all by Bouchard of France, at the International Congress of Medical Science held in London in 1881. He showed that he had met with bacilli in the urine and he stated that the micro-organism had all the morphological characteristics of the germ found in the blood of the same patients. Of 65 cases examined he found the bacilli in the urine of 21.

Five years later the works of Huppe and Seitz were published. The former examined the urine of 18 cases out of which he had only 1 positive result. Seitz's examination gave a larger proportion, for out of 7 cases he found the bacilli in the urine of 2.

Following on these, many independent observations were made by investigators in different countries. In 1887 M. Berlioz isolated and cultivated Eberth's bacillus in 2 out of 14 cases.

In 1888 M. Koniäiev, in Russia, worked at this question and of 20 patients attacked with typhoid fever, he discovered the specific germ in the urine of 3 of these.

In Germany in the same year, Neumann in a monograph on the bacteriology of urine made an important communication. In 23 cases he obtained 6 positive results. Again in 1890 he added 11 out of 48 cases which presented the bacillus typhosus in the urine. He pointed out that frequently the urine which contained the bacilli was turbid, because of the large number of micro-organisms present. He thought that he had probably failed to detect them in those specimens in which they were in small numbers, and he considered that they were finally removed from the bladder mechanically. He stated that he usually found the organism in pure culture and the

urine was always acid.

Karlinski found that 21 cases presented the bacillus out of 44 which he examined thus obtaining almost 50% of positive results. 38 specimens were taken during life and 6 after death. In all of these albumin was present and persisted for some time. When albuminuria was transient no bacilli were found. The earliest day on which Karlinski found the bacillus in the urine was the 3rd, and in the stools, the 9th.

In 1895 in an investigation into the cause of pyuria occurring in the course of enteric fever, Blumer found the bacillus present in 2 out of 60 cases examined, of which number 10 had pyuria. I shall refer again more fully to the work of these two observers.

In 1892 Silvestrini found the bacillus typhosus in 100 per cent of his cases i.e. in 7 out of 7, while M. Baart de la Faille read a communication before the Faculty of Medicine of Utrecht in which he stated that he had examined the urine of 27 cases of enteric fever, four of which contained Eberth's bacillus, while in 4 other cases the bacillus coli communis was present. In 6 out of 7 cases Wright and Semple obtained the typhoid bacillus. They refer to the work of Wathelet who had examined the

stools for the typhoid bacillus and in 12 cases involving 24 examinations the bacillus had been found only 4 times. This led Wright and Semple to infer that typhoid fever is spread more by the urine than the faeces, and from the presence of bacilluria and roseola they brought forward the theory that the disease was really one of general infection just like malaria and anthrax, and that it was possible to diagnose the condition from an examination of the urine.

Unfortunately many of these early investigations cannot be regarded as at all accurate, because it was only in 1885 that Escherich discovered the bacillus coli communis and separated it from the bacillus typhosus, and faulty differentiation of these two organisms would account for the high percentage obtained in many cases.

They had not the means of distinguishing the typhoid bacillus from the colon group of organisms. They found a bacillus which was motile, rod-shaped and which grew on certain media very much like typhoid bacilli, but the tests used were inaccurate and insufficient. It was only in 1896 that Widal gave us a reliable means of separating Eberth's bacillus from the colon group of bacilli.

In more recent times much work has been done on this subject by Petruschky, Gwyn, Horton Smith

and Richardson and these open up a new period in the history of typhoid bacilluria. In 1897 Horton Smith read a communication before the Royal Medical and Chirurgical Society, London, and in this he declared that he had found bacillus typhosus in the urine of 3 cases of the 7 examined by him. This involved 61 observations. As soon as the case was diagnosed the urine was taken and examined every second or third day till about a week after the temperature had become normal. The urine was not drawn off by the catheter, as some of the previous experimenters had done, but was passed by the patient directly into a sterilised flask. To this method there was one exception and that was in the case of a woman. All the other cases were males. The procedure adopted by Horton Smith then was that (a few urines were filtered) a drop of the urine was examined under the microscope and a stained preparation was made. Then one or two drops were put on to a plate of jelly which had solidified, and 20 drops were put on to another plate, these being incubated at 20°C and examined at the end of 24, 48 and 72 hours.

Suspicious colonies were further examined and gelatine stroke cultures and shake cultures were made. These in their turn were incubated and if gas were found no further examination was carried out.

If no gas were got the organism was grown in milk and broth and a Widal reaction was looked for. Seven cases were examined and in 3 of these typhoid bacilluria was present. With regard to the time in the course of the case when this condition was got, Horton Smith never found the bacillus present before the third week. In one case it was found on the 39th day notwithstanding the fact that 10 observations were made previous to this. Smith emphasised the fact first pointed out by Neumann that the bacilli may be present in such enormous numbers that the urine is rendered turbid. He found that the condition of bacilluria may in some cases be known to be present, because if a test tube with some urine in it be shaken and held up to the light a peculiar shimmer is seen, such as is seen in a broth culture of the organism. The conclusions which he came to as a result of his research are given as follows.

1. Bacillus typhosus occurs in some urines, not in all.

2. When they occur they are in considerable numbers, a plate made with ½ c.c. being sufficient to detect them.

3. The bacilli appear during the third week or later and therefore can rarely be of assistance in diagnosis. If bacilli are got earlier they will

probably be bacillus coli.

4. The urine should be disinfected.

In 1899 Horton Smith published a second memoir in which he drew attention to the part played in the dissemination of typhoid fever by the urine and faeces respectively. Of 12 urines examined he found the typhoid bacillus in 4. Of these 4 one was a case with pyuria occurring on the 30th day of the disease, continuing through a relapse of 15 days duration and persisting for a few days into convalescence. The bacillus was found in large numbers. In this case the stools were examined four times and on each occasion a negative result was obtained.

The work done in regard to the presence of the bacillus in the faeces seems to show that the dejecta contain that organism early in the disease.

Horton Smith examined 29 stools and found the bacillus in each, but only during the first two weeks.

Pollak of Prague in 1896 examined 13 cases, the faeces of each of which contained the typhoid bacillus during the first and second week of the examination.

Jemma of Genoa investigated 20 cases and in 100 per cent he found the specific organism during the first two weeks of the disease.

Richardson found it at the first examination in 4 cases, on the 5th, 11th, 11th and 12th day respectively. In one case he failed to find it at the first examination on the 6th day.

The third series of observations made by Horton Smith and published in 1900 consisted of 45 cases of enteric fever. In 17 of these the bacillus typhosus was found in the urine. Of the 17 cases 6 had been selected because of the urine having some peculiar characteristic: the others were chosen at random. The figures thus corrected give a percentage more in accordance with other observers. It is important to note that the organism was found to be present in one case as early as the 13th day. It is, however, exceptional to find it so soon and most observers mention the 3rd or 4th week as being the time when it is most likely to be found. Its appearance may be delayed till well on in convalescence and many days after the temperature has reached normal. In 15 cases recorded by Horton Smith the date of the first appearance is given in 9 of them as follows:-

Day of disease		
15	-	twice
24	-	once
32	-	do
36	-	do
39	-	do

Day of disease after defervescence		
5	-	once
6	-	do
10	-	do

That the bacilli are present in the urine for a varying time is shown by the following figures.

Duration of bacilli in the urine of 9 cases:-

8, 21, 30, 70, 13^{x}, 18^{x}, 19^{x}, 34^{x}, 40^{x} days, where x indicates that the bacillus was present for at least that number of days, but the examination of the urine was not carried out further.

The presence of albumin in the urine is referred to by Smith. This, he finds, is not always present and there appears to be no connection between these two conditions. When present it may be got as a mere trace or in large amount.

In one case haematuria was present.

Pyuria, on the other hand, was found in 50 per cent of the cases and the pus may show itself as a big deposit or merely as a few cells detected by the aid of the microscope and giving rise to no symptoms whatever. Obvious typhoid cystitis is very rare indeed, the reason being that if the vesical mucous membrane be normal and if the urine be passed at the usual intervals no cystitis will occur, even if bacilluria be present. On the other hand, however, if the bladder wall be damaged in any way, e.g. by a foreign body or if residual urine be present, or if retention occur, as one might expect in a person suffering from a severe attack of enteric fever, then

the conditions, in which cystitis may be set up, exist.

Melchior, in 1897, showed that if a rabbit be taken and if 1c. c. of broth culture of the typhoid bacillus be injected into the bladder, no cystitis is set up, but merely typhoid bacilluria lasting several days. When retention is artificially produced by ligaturing the penis for a few hours cystitis follows.

The bacilli were present in such large numbers that in 12 out of 14 cases the urine was rendered distinctly turbid and a shimmer was seen when the urine was held up to the light and shaken.

In an article in the John Hopkins Hospital Bulletin Gwyn draws attention to the great danger incurred through the omission of disinfecting the urine of typhoid patients. He points out that up till 1899 no proper systematic disinfection of that fluid was carried out. He dwells on the fact that in many cases the bacilli are present in enormous numbers, he himself having calculated as many as 500 million in one cubic centimetre in one case. This shows the excessive quantity which may be passed by a patient at one time. In other words a daily amount of urine would contain 500,000 million organisms and according to calculation such a urine diffused in 10 cubic

metres of water or sewage would give 50,000 colonies of bacilli per one cubic centimetre of water or sewage.

Gwyn thinks that in from 20 to 30 per cent of all cases Eberth's bacillus is present and that, as a rule, it is found in pure culture. It may persist for months or years. He reports one case where he found the bacilli in the urine of a patient four years after an attack of enteric fever. Gwyn does not mention the number of cases examined by him, but in 8 he found the specific germ and one noteworthy feature of these cases is that in 7 of them, there was pyuria, while in 5 of these the pyuria was present along with bladder irritation. This seems an abnormally high proportion of both these conditions when compared with the figures of other observers. The time when the bacillus was found is stated as follows:-

In 3 cases in the 3rd week
1 case " " 5th "
1 " " " 6th "
1 " " " 3rd month
1 " " " 4 year

In one case the patient suffered from nephritis.

An interesting point is stated by Gwyn in reference to the possibility of diagnosing the presence of enteric fever from an examination of the

urine. In two of his cases he was at first unable to obtain a Widal reaction, although all the signs and symptoms pointed to the cases being enteric. On examination of the urine in each case typhoid bacilli were found. The explanation given is that the Widal reaction is long delayed because of many bacilli being in the blood as is the case in typhoid septicaemia. Therefore it seems that in that class of case the urine should be searched for the organism as an aid to diagnosis. Gwyn finds that there is usually a trace of albumin in the urine along with the bacilli, but in most of his cases pyuria was present and this would account for the albumin. In two of his cases, however, albumin was present in large amount. As shown by Neumann he finds it possible to suspect the presence of bacilli in freshly voided urine by its turbidity and its acid reaction. This was seen in all but one case.

The treatment adopted by Gwyn was irrigation of the bladder and the administration of urotropine, but I shall refer to this again.

MM. Levy and Gissler have contributed to the subject in question. In examining 22 cases they found that 10 had specific bacteriuria and Schüder had 5 positive results from 22 cases.

More recently MM. Lesieur and Mahaud made

observations in 15 cases and from these obtained 7 with bacilluria. The results of these two observers are interesting because in two of their cases they found the bacillus as early as the 10th day.

Herbert obtained 18 positive results out of 98 cases, while simultaneously with but independent of Horton Smith's work, Besson in France had undertaken the research. In 33 cases investigated by him, examination of the urine revealed the presence of Eberth's bacillus in 6. He maintained that the bacillus was found only when albumin was present in the urine and that when the albumin disappeared it was impossible to separate out any bacilli. He maintained that the albuminuria is brought about by the elimination of the specific germ and the greater the elimination of bacilli the more intense the nephritis.

Two years later Schichhold published the result of his research and stated that the bacillus is got only when nephritis is present.

Against these, however, Neumann pointed out that the albuminuria was less frequent than the bacilluria and more recent works point in the same direction. That the two conditions may be got together has not been denied, but Blumer and others

have made out that albuminuria is not more frequently got in cases with bacilluria than in those uncomplicated by the elimination in the urine of the specific microbe.

Vincent states in La Semaine Médicale that he has obtained a positive result in 9 out of 46 cases. Albuminuria is not by any means a constant concomitant. He was able to isolate the bacillus generally from the eleventh to the seventeenth day, and he emphasises the fact that the urine may contain many organisms well on in convalescence and after complete recovery. In two of his cases the urine was infected up to the 19th and 37th day respectively, after cure. He found that some days the bacilli are in enormous numbers, while on other days they are present in such small quantity that they are found only with difficulty. He thinks that this phenomenon coincides with the degree of acidity of the urine.

Vincent, two years previous to his work on typhoid bacilli in the urine, published two cases of haemorrhagic cystitis due to typhoid bacilli. This is a very rare condition, for out of 1200 cases of enteric fever he has observed only two in which it was present. The patients were 21 and 22 years of age with no previous urinary trouble. In the 2nd week they were suddenly seized with severe pain over the

pubis, pain on micturition and frequency of the act. The urine contained pus and blood along with bacilli in great numbers, which on cultivation were found to be typhoid bacilli.

About the same time MM. Lévi and Lemierre reported a similar case in a man 24 years of age. They drew attention to the possibility of bacillus typhosus being present in the urine with or without symptoms of cystitis.

Blumer in 1895 investigated pyuria as a complication of typhoid fever. He found the condition in 10 out of 60 cases which he examined. Of these 10 only 2 revealed the bacillus typhosus, one in pure culture, the other being present along with the colon bacillus. He pointed out that the quantity of pus varies much and that there is no relation between pyuria, typhoid bacilluria and rose spots, as Konjajeff tried to make out. Konjajeff said that the bacillus typhosus in the urine is a sign of lymphomata in the kidney and that the lymphomata are found about the same time as the rose spots appear on the skin.

When the typhoid bacilli were present the pus first appeared, in one case, between the 5th and 6th week: in the other case it appeared on the day of

the patient's death, but it is not stated how long she had been ill.

That the presence of pyuria in enteric fever is not necessarily due to the specific germ is brought out in the investigations of Blumer. Only 2 out of 10 urines contained that organism, while the colon bacillus was found in pure culture in 6 urines and in one along with typhoid bacillus. Staphylococcus pyogenes albus was present in one urine, and in the tenth a coccus which was not identified was got.

Petruschky examined 50 cases and obtained 3 positive results. These three urines were distinctly turbid. In one no albumin was present. In the others it was got only as a trace. One case revealed the presence of bacilli ten days after convalescence was begun and they persisted four weeks. In another bacteriuria began 6 days after defervescence. Petruschky calculated that as many as 170 million bacilli were present in 1c.c. of one specimen of urine. He relates an unfortunate incidence as happening to a ward sister who drank a small quantity of urine which had been passed by a distressed patient into a tumbler which was lying at hand. Twelve days later she was attacked by the fever.

Richardson made an exhaustive study of this

question. In a series of 38 cases 9 were affected with typhoid bacilli in the urine. In 5 of these he was able to cultivate the organism at the first examination i.e. on the 23rd, 33rd, 34th, 38th and 38th day. The earliest day on which Richardson found it was the 15th, but in the majority of his cases it was not found till after the 30th day. Of 7 discharged from hospital as well, 5 still had the bacillus in the urine and in 2 of them it persisted for at least 10 days. The presence of the bacilli was practically always accompanied by albuminuria, and he went the length of stating that "we can say that a non-albuminous urine very probably contains no typhoid bacilli."

According to Richardson the post-febrile polyuria may aid in the expulsion of bacteria, butin two cases which passed on an average 70 and 80 ounces daily no appreciable diminution in their number took place. He found that there was a greater tendency to relapse and complication if typhoid bacilli were found in the urine.

Of 29 negative cases 8 had bacteria of other kinds, but of these, 4 had been catherised or operated on and therefore the infection may have been from without. In 4 the bacillus coli was found, 2 contained a diplococcus, and in the 7th there was a

diplococcus followed by the colon bacillus, while in the 8th steptococcus and the colon bacillus were got together.

In one case with typhoid bacilluria Richardson washed out the bladder with 2% boracic solution. It was retained for 3 hours, but it had no effect on the organism. He then used 1 in 7000 corrosive sublimate solution which was not retained at all. It had a most beneficial effect, because for 30 days no bacilli were discovered.

In his second series of 66 cases examined more especially to test the actions of urotropine on the typhoid bacilli, he found the bacillus in 14 of them. The earliest dates on which he found Eberth's bacillus, in this series of cases, were the 12th, 14th, and 15th days of the disease.

The results of the use of urotropine I shall refer to again.

Lewis thinks that the more severe the case the more likelihood there is of the urine being infectious. He examined 45 cases involving a large number of specimens and of these he obtained only one which contained the typhoid bacillus. He thinks that if all the mild cases and all the severe cases were taken and examined only 10 per cent would show the specific germ in the urine.

He refers to Kuhnan's researches on the blood of typhoid patients where he found the bacillus in 25% of the cases. In order to reach the urine, the bacillus, he holds, must be in the blood and it is not likely that every case which has the organism in the blood will have it in the urine, since the most probable theory is that the presence of the bacillus in the urine is due to a stray microbe finding its way into the bladder and there multiplying and not due to a renal elimination. According to Lewis there are two periods in the course of the disease in which this condition may be expected. These are:-

1. Got in severe cases: generally commencing during the height of the disease and seldom in the first fortnight: associated with albuminuria often with pyuria or haematuria: diminishing as the urine contains less albumin and disappearing in a few days or weeks after the albumin.

2. Got in severe or mild cases: begins in later stage, maybe after the temperature is normal: persisting into and during convalescence, even for weeks or months without causing severe symptoms: albumin is not a necessary accompaniment: cystitis is not constantly present.

II

The work on this subject which I carried out and which I am now about to detail, was done in the laboratory of the Edinburgh City Hospital. For the notes of the cases I am indebted to Dr. Claude B.Ker, Medical Superintendent of the hospital. I examined the urine of 15 cases and this entailed close on 100 specimens. The cases were taken at random from the wards and none was selected because of any symptom of urinary trouble, or because of a suspicious looking urine.

The procedure which, as a rule, I adopted was as follows. The patient was got to pass the urine directly into a sterilised flask very shortly before the examination was conducted. A small quantity of this was then poured into a sterilised test-tube and centrifuged. A sterilised pipette was used and with this some urine from the bottom of the test-tube was taken along with any deposit which might be present. From 4 to 8 drops were then put on to a plate of agar or jelly and incubated at 37° or 20° C. At the same time a drop of the fluid was examined microscopically and if bacilli were present a stained preparation was made. After 24 hours, if agar, or

3 to 4 days, if jelly, the plates were examined. If any colony looked at all suspicious subcultures were made from it. The media used were sloped agar or jelly, broth, litmus milk and glucose jelly.

Then if an organism was found which was morphologically like bacillus typhosus - presenting forms of different lengths, very actively motile, giving no indol reaction, not producing coagulation of milk even after many days incubation, and producing only a slight acid reaction and not forming gas in glucose jelly then the presumption was that we were dealing with bacillus typhosus. But over and above these tests, a Widal reaction was looked for in each case and unless this was obtained the organism was not considered to be Eberth's bacillus. The method which I employed was that recommended by Delépine. A young agar culture was used and the dilution was 1 in 50. With all these tests it was possible to say whether an organism was bacillus typhosus or not and to eliminate the colon bacillus which might very well be a source of error.

From the 15 cases I examined I was able to obtain the organism in the urine of 8 of them, a few notes from the history of which I now give.

No. 1. J.C. aged 44 years: admitted on the 28th October with the history of being out of sorts for 3 weeks: confined to bed for 2 weeks suffering from pain in the back and head, shivering and diarrhoea. No abdominal pain or epistaxis. On admission - tongue furred and suggestive of typhoid fever: a few suspicious spots: stools very offensive: Widal reaction obtained on 31st October. Urine showed no diazo or albumin. A mild case of enteric.

No. 2. J.W. aged 21 years: admitted on 12th November 1904 on the 26th day of the disease. Patient had been ill for about a month with headache, abdominal pain, cough and epistaxis: no diarrhoea. On admission - large pupils: malar flush: glazed raw tongue: dicrotic pulse: abdomen flat and soft: some rose spots present: spleen not enlarged. The temperature reached normal on the day after admission. Widal reaction got on 15th November. A moderately severe case.

No. 3. J.B. aged 28 years: was admitted on 10th October 1904 on the eighth day of the disease. Patient had not been feeling well for one week and had been in bed for 5 days with pain in the back and in the abdomen: complained of shivering, diarrhoea

and bleeding at the nose.

On admission - looks like a case of enteric: pupils normal: tongue dry in the centre: abdomen full but not very tense, not tender: spleen enlarged to anterior axillary line: pulse dicrotic: stools light coloured and constipated: typical spots present. Patient is sharply ill. Diazo reaction obtained in urine. Widal reaction got on 15th October.

No. 4. M.B. aged 28 years: admitted on 28th September: had been ill 10 days: had felt sick and tired: no epistaxis, pain or diarrhoea.

On admission - patient is flushed: pupils small: tongue is suggestive: abdomen is tumid not tense or tender: good rose spots: spleen enlarged: pulse tends to dicrotism.

Patient was most seriously ill and in a very critical condition for some time. Diazo reaction present. Widal reaction obtained on 4th Oct.

No. 5. F.G. aged 39 years. Was admitted on 22nd October. Had been ill for a fortnight with pain in back and abdomen: had suffered from diarrhoea: no epistaxis.

On admission - pupils large: malar flush:

suggestive tongue: abdomen large and tumid: several suspicious but not typical spots: spleen decidedly enlarged: pulse is dicrotic: a history of alcoholism got. On the 28th October patient had a severe haemorrhage from the bowel and his pulse bagan to fail: patient became maniacal and required sedatives. Temperature reached normal on 31st October, but on 8th November it rose and patient had a severe relapse lasting till the 25th November. During the relapse he became maniacal and unmanageable and he continued in this state for several days.

Urine revealed albumin and the diazo reaction was obtained on several occasions. Widal reaction was got on the 25th October.

This was a very severe case of enteric.

No. 6. N.W. aged 26 years. Admitted on 18th October on the 5th day of the disease: patient had felt very tired and had suffered from severe headache for 5 days: took to bed feeling very ill.

On admission - patient is very ill: malar flush: pupils dilated: tongue is furred and dry: abdomen soft not tumid: rose spots typical: spleen not much enlarged: pulse dicrotic. Albumin got in early stage and Ehrlich's reaction also: Widal reaction obtained on 20th October.

22nd October: patient is nervous and excited, requiring bromide and chloral: most profuse eruption of rose spots: spleen much enlarged.
25th October: patient is very sharply ill: delirious and noisy: an exceptionally profuse eruption on trunk, arms and legs: tendency to diarrhoea.
27th October: still has a poisoned appearance: tongue improving.

This was a most severe septicaemic case.

No. 7. A.F. aged 34 years. Admitted on 3rd December: had been ill for a fortnight with severe headache, shivering, pains all over, diarrhoea, epistaxis and want of sleep.

On admission - patient has a flushed appearance: pupils normal: tongue typical: abdomen full: spots are suspicious: spleen slightly enlarged: pulse soft.
5th December abdomen softer: spleen enlarged to greater extent: more suspicious spots: pulse dicrotic: stools dark and constipated. Widal reaction obtained. Diazo reaction and albumin got in urine. Temperature settled on 19th December, but a relapse set in on 21st December and continued till the 8th January.

Patient suffered from a very severe attack.

No 8. J.P. aged 40 years. Had been ill for 3 weeks: took to bed on 13th November and was admitted on 17th November: felt very ill with headache: pains in back and abdomen and shivering: no diarrhoea or epistaxis. On admission - patient looks thoroughly exhausted: pupils normal: tongue is very suggestive: large prominent abdomen somewhat tense: spleen enlarged: stools typical: one suspicious spot. Ehrlich's reaction and albumin obtained early. Widal's reaction on 18th November. Temperature settled on 9th December. This case, which was a moderately severe one, was complicated with phlebitis from the 3rd December.

The following are short notes of the seven cases of enteric in which I was unable to isolate the typhoid bacillus from the urine.

No. 9. A.P. aged 6 years: admitted on the 25th October with a history of headache, shivering, abdominal pain and constipation: no epistaxis: he had been ill for a fortnight. On admission - he is flushed: pupils somewhat dilated: tongue suggestive: abdomen full, not tense: no rose spots: spleen somewhat enlarged. No diazo reaction or albumin in urine: Widal reaction got on 25th October. A case of moderate severity.

No. 10. M.F. 14 years: admitted on 12th October with the history of not feeling well since the 3rd October, and of headache, pain in the back, sick and vomiting: no abdominal pain or diarrhoea.

On admission - patient looks like a case of enteric: big pupils: tongue slightly furred: abdomen tumid and tense not tender: spleen enlarged: pulse dicrotic. A few days after admission a few rose spots appeared. Diazo reaction got but no albumin in urine. Widal reaction obtained on 15th October. A mild case of typhoid fever.

No. 11. C.W. admitted on 20th October, on the 21st day of the disease, complaining of headache, intense pain in the abdomen, diarrhoea, loss of appetite and vomiting of three weeks duration. No epistaxis. On admission - patient is pale and puffy, with dilated pupils: tongue very suggestive: abdomen enormously distended and tense: no spots: spleen doubtful because of distension. Temperature settled two days later. No albumin or diazo reaction got in urine. Widal reaction on 25th October. This was a mild case of enteric.

No. 12. J.C. aged 6 years. Was admitted on 17th December on the 15th day of the disease, with the

history of inclination to be sick, and epistaxis: no vomiting, abdominal pain or diarrhoea.

On admission - patient looks like one suffering from enteric: pupils normal: heavy furred tongue: abdomen tumid and soft: no spots present: spleen considerably enlarged: stools constipated. No albumin or Diazo reaction obtained. Widal reaction got on 19th December. A mild case of typhoid fever.

No.13. M.B. 11 years of age: admitted on 11th October: had been ill since 2nd October with headache, abdominal pain, sickness, vomiting, diarrhoea and epistaxis. On admission - patient has a typical appearance: dilated pupils: tongue raw and dry: abdomen tumid: one or two suspicious spots: spleen is enlarged. Ehrlich's reaction and albuminuria during the first week. Widal reaction got on 15th October.
A very severe case.

No. 14. J.B. aged 22 years: admitted on 10th November on 14th day of the disease complaining of pain in the back and head, sickness, vomiting and diarrhoea: no abdominal pain or epistaxis.

On admission - looks exhausted: tongue glazed and furred: pupils normal: abdomen tumid but

soft: some typical spots present: spleen enlarged: pulse dicrotic: Widal reaction got on 15th November. Albuminuria and diazo reaction present.
A very severe case.

No. 15. L.M. aged 28 years: admitted on 12th November on the 21st day of the disease, with the history of headache, sickness and diarrhoea: no abdominal pain or bleeding at the nose: not sleeping at all well. On admission -patient has flushed appearance: tongue moist but suggestive: abdomen full not tender: no spots: spleen is slightly big: pulse dicrotic. Diazo reaction and albumin in urine got early. Widal reaction on 15th November.
A moderately severe case.

In none of the eight positive cases was I able to isolate the bacillus from the urine in the early stages of the disease. The earliest day on which I found it was the 28th, but it is quite probable that the urine was infected prior to this, because it was at the first examination that I discovered it. The 59th was the latest day of the disease on which they were first found, although three observations were made previous to their discovery in this case.

The following table (No.I) gives the day of the disease on which the bacillus typhosus was first found and the day on which it was last found. The x signs indicate that no observations were made after this day.

Table No. I

Case No.	B.T. discovered on	B.T. persisted until
8	28th day of disease	43rd day of disease
3	30th " " "	36th " " "
1	32nd " " "	55th " " "
7	41st " " "	60th " " "
6	42nd " " "	72nd[x] " " "
2	43rd " " "	-
4	54th " " "	81st[x] " " "
5	59th " " "	85th " " "

In no case was there a distinct deposit of pus, but in 3 out of the 8 which contained typhoid bacilli, there were a few pus cells along with some squamous epithelial cells which were in greater quantity than normal. In these there was a slight trace of albumin, probably such as could be accounted for by the pus present. No casts were seen in any of these three urines. In a fourth case (No. 5) albumin, hyaline and granular casts were found prior however to the discovery of the specific bacillus by about 5 weeks, and at only one observation were these found along with the bacillus.

The following table (No.II) shows in detail the results of the examination.

Table No- II. Positive Results.

Case. No.	Urine Examined.	Day of Disease.	Organisms Found.	Albumin &c.	Severity.	Rose Spots.
I	November 4	29	Staph Pyog.Alb.	No Albumin	Mild.	Suspicious Spots.
	" 7	32	B.T.& St.Py.Alb.	"		
	" 16	41	B.T.	"		
	" 30	55	B.T.	"		
	December 8	63	St.Py.Alb.	"		
	" 14	69	St.Py.Alb.	"		
II.	November 14	28	Bac.Coli.Com.	"	Moderately Severe.	Some Spots
	" 29	43	B.T.	"		
	December 1	45	Staph.Pyog.Alb.	"		
	" 9	53	Bac.Coli.Com.	"		
	" 13	57	Bac.Coli.COM.	"		
III.	November 1	30	B. T.	"	Very Severe	Good Spots.
	" 7	36	B. T.	"		
	" 17	46	Staph.Pyog.Aur.	"		
	" 25	54	Staph.Pyog.Aur.	"		
	" 30	59	Staph.Pyog.Aur.	"		

Table No. II. (Continued).

Case. No.	Urine Examined.	Day of Disease.	Organisms Found.	Albumin &c.	Severity.	Rose Spots.
IV.	November 4	47	Bac.Coli.Staphy.Py. Aur.	No Albumin.	Very Severe.	Good Spots.
	" 11	54	B.T.Staph.Py.Aur.	Albumin pus and squam.epithelium.		
	" 23	66	B.T.	Albumin & Pus.		
	" 28	71	B.T.	Albumin & Pus.		
	December 1	74	B.T.	No Albumin.		
	" 8	81	B.T.	"		
V.	October 27	20	Bac.Coli.Com.	Albumin & Casts.	Very Severe Relapse.	Suspicious Spots.
	" 29	22	Bac.Coli.Com.	" "		
	November 17	40	Staph.Pyog.Aur.	" "		
	December 7	59	B.T.& B.C.C.	" "		
	December 12	64	B.T.	No Albumin.		
	" 17	69	B.T.	"		
	" 20	72	B.T.	"		
	" 22	74	St.Pyog.Aur.	"		
	January 2	85	B.T.	"		
	" 9	92	B.C.C.	"		
	" 17	100	B.C.C.	"		

Table No. II. (Continued).

Case. No.	Urine Examined.	Day of Disease.	Organisms Found.	Albumin &c.	Severity.	Rose Spots.
VI.	October 27	14	Bac. Coli. Com.	No Albumin.	Severe Septicaemia.	Most profuse Rash.
	" 31	18	Bac. Coli. Com.	" "		
	November 24	42	B.T.	Albumin & few Pus Cells.		
	December 6	54	B.T.	" "		
	" 10	58	B.T.	" "		
	" 13	61	B.T.& B.B.C.	" "		
	" 14	62	B.C.C.	No Albumin.		
	" 19	67	B.C.C.	"		
	" 24	72	B.T.& B.C.C.	"		
VII.	December 30	41	B.T.	No Albumin.	Very Severe. Relapse.	Suspicious Spots.
	January 2	44	B.T.	"		
	" 5	47	—	"		
	" 9	51	B.T.	"		
	" 14	56	B.T.	"		
	" 17	58	B.T.	"		
	" 19	60	B.T.	"		
	" 23	64	Staph.Pyo.Aur.	"		

Table No. II. (Continued).

Case. No.	Urine Examined.	Day of Disease.	Organisms Found.	Albumin &c.	Severity.	Rose Spots.
VIII.	November 24	28	B.T. St.Pyog.Alb.	Albumin, Pus & Squam. Epithelium.	Moderately Severe.	Suspicious Spots.
	December 5	39	B.T. St.Pyog.Alb.	" "		
	" 9	43	B.T. St.Pyog.Alb.	" "		
	" 13	47	St.Pyog.Alb.	No Albumin.		
	" 16	50	St.Pyog.Alb.	"		
	" 28	62	St.Pyog.Alb.	"	Phlebitis. from 3rd.Dec.	
	January 3	68	St.Pyog.Alb.	"		

In the seven negative cases the organisms found were the bacillus coli communis, staphylococcus pyogenes aureus and albus, bacillus pyocyaneus, either alone in pure culture or along with another organism.

The bacillus coli was found in the urine of five cases, while the bacillus pyocyaneus was got in four cases, three of whom were females, the fourth being a boy.

The negative results are given in Table No. III.

Pus was present in only one of these seven cases (No. 10) and the urine of this patient contained the bacillus coli in pure culture. In 3 of the 8 cases the typhoid bacilli were in such numbers that they were readily seen when a drop of the urine was examined under the microscope, but a shimmer described by some was not observed in any case. From some urines the colonies obtained on cultivation were very profuse, while in others there were very few, and the same phenomenon was observed with the different specimens from the same patient - one day the bacillus was readily obtained and at the next examination perhaps only one or two colonies were evident.

While a small quantity of pus was obtained in three positive cases (i.e. 42.8%) yet none of the patients complained of any urinary symptoms and there was an entire absence of cystitis.

Table No. III. Negative Results.

Case. No.	Urine Examined.	Day of Disease.	Organisms Found.	Albumin &c.	Severity	Rose Spots.
IX.	November 16	40	Staph.Pyog.Alb.	No Albumin.	Moderately Severe.	None
	December 6	61	" " "	"		
	" 9	64	" " "	"		
X.	November 14	43	Bac.Coli.Com.	Albumin pus & squam. epithelm.	Mild.	Few Spots.
	" 28	57	Bac.Coli.Com.	" "		
	December 7	66	Bac.Coli.Com.			
XI.	November 1	33	Staph.Pyog.Aur. and Alb.	No Albumin.	Mild.	No Spots.
	" 3	35	" "	"		
	" 24	56	" "	"		
	December 6	68	" "	"		
	" 10	72	" "	"		
XII.	December 19	17	Staph.Pyog.Aur.	No Albumin.	Mild.	No Spots.
	" 22	20	S. P. A.	"		
	" 24	22	S. P. A.	"		
	" 28	26	S.P. A.	"		
	January 2	31	S. P. A.	"		
	" 9	38	S. P. A	"		
	" 14	43	S. P. A. & B. Pyo.	"		

Table No. III. (Continued).

Case. No.	Urine Examined.	Day of Disease.	Organisms Found.	Albumin &c.	Severity.	Rose Spots.
XIII.	November 3	33	Bac.Coli.Com.	No Albumin.	Very Severe	Good Spots.
	" 11	41	B. C. C.	"		
	" 29	59	B. C. C.	"		
	December 8	68	B. C. C.	"		
	" 12	72	B. C. C.	"		
	" 14	74	B. C. C. & B. Pyo.	"		
	" 17	77	B. C. C.	"		
	" 27	87	B. C. C.	"		
XIV.	November 29	33	Bac.Coli.Com. & B.Pyo.	"	Very Severe.	Good Spots.
	December 8	42	B.C.C. & B. P.	"		
	" 12	46	B. C. C.	"		
	" 16	50	B. C. C.	"		
	" 20	54	B. C. C.	"		
	" 27	61	B. C. C.	"		
	January 3	68	B. C. C.	"		
XV.	November 25	34	Bac.Coli. & B.Pyo.	"	Moderately Severe.	No spots.
	December 6	45	B. C. C. & B. P.	"		
	" 10	49	B. C. C.	"		
	" 16	55	B. C. C.	"		
	" 20	59	B. C. C.	"		
	" 27	66	B. C. C.	"		
	January 3	73	B. C. C.	"		

III

From a study of the literature on typhoid bacilluria it is apparent that among the cases examined and recorded since 1897 there is no great uniformity in the proportion of those exhibiting this condition. The proportion varies from 2.2% given by Lewis up to 46.6% found by Lesieur and Mahaud. Why there should be such a great difference in the positive results is very difficult to explain except that the methods of examination may not have been the same or conducted with the same care. In some observations the urine may have been examined only in the early stages prior to the appearance of the organism and few of the investigators make any mention of centrifuging the urine, a procedure which I adopted in all cases.

Table No. IV summarises the results obtained since 1897.

Table No. IV.

Name	Year	Cases Examined.	Positive. Results.	Percentage.
Horton Smith.	1897	7	3	42.8
"	1899	12	14	33.3
"	1900	45	17	37.7
Levy and Gissler.	1897	22	10	45.4
Schüder.	1901	22	5	22.7
Lesieur and Mahaud.	1903	15	7	46.6
Herbert.	1904.	98	18	18.3
Besson.	1897	33	6	18.1
Vincent.	1903	46	9	19.5
Richardson.	1898	38	9	23.6
"	1899	66	14	21.2
Petruschky.	1898	50	3	6 .0
Lewis.	1901	45	1	2.2
		499	106	
Dods Brown.	1904	15	8	53.3

The average percentage obtained from the results of the observations made by these 12 investigators works out at 21.24%. Another striking feature in these works is the great disparity in the time of the appearance of the bacilli.

In recent times M M. Lesieur & Mahaud state that in two of their cases they found the organism on the 10th day, while Vincent gives the usual period as from the 11th to the 17th day. The earliest date on which

Smith isolated the bacillus was the 13th, but he says that most positive results are got in the third week. On the other hand, in one case it was 14 days after the temperature had reached normal that the bacillus was found and Schüder had one case in which he obtained the bacillus as late as the 21st day of convalescence. As stated above Gwyn's observations point to the fact that the specific bacilluria may show itself in the 3rd week or not until the 3rd month after the onset of the disease. Richardson was able to demonstrate their presence in the urine early in the disease in several cases. Thus in one case it was found on the 12th day, in a second on the 14th day and in two he isolated it on the 15th day.

The persistence of the bacilluria is just as variable as is the original appearance of the organism. In one of Petruschky's cases it was present for 7 weeks after the subsidence of the fever, while in another it persisted 6 weeks after cure. Vincent records two cases in which the bacillus typhosus was found on the 19th and 37th day, respectively, after the patient was considered cured. M. Busing relates a case where the patient had taken on an appearance vigorous and strong, and yet the organism was present in the urine 6 months after recovery. In three of Richardson's cases the organism was present in the urine on the 61st, 72nd and 78th day, respectively,

but further examination was not carried out. Houston recorded a case, which bears a great similarity to one published by Gwyn, in which cystitis due to the typhoid bacillus persisted for three years after an attack of enteric fever.

The table below (No.V) shows at a glance the earliest day of the disease on which I found Eberth's bacillus and the length of time it persisted. It also shows the day on which the temperature reached normal.

Table No.V

Case No	B.T. discovered on	Temp. normal	B.T. persisted until
3	30th day of disease	29th day of disease	36th day of disease
1	32nd " " "	28th "	55th "
7	41st " " "	50th[c] "	60th "
6	42nd " " "	35th "	72nd[x] "
2	43rd " " "	28th "	-
4	54th " " "	39th "	81st[x] "
5	59th " " "	47th[c] "	85th "

c Relapse Temperature Normal

The x sign denotes that the urine was not examined after this day.

Albuminuria

Seitz, Besson and Schichhold independently stated that bacilluria and albuminuria always go together and that without albuminuria there cannot be bacilluria.

Besson found that when the albuminuria disappeared he was unable to find any typhoid bacilli. Schichhold went further for he held the opinion that the presence of bacilli in the urine was indicative of nephritis and the more severe the nephritis the greater the number of organisms eliminated.

Neumann, on the other hand, found that the presence of albumin was less frequent than that of the bacteria, while Horton Smith and others state that albumin is not more frequent in cases with bacilluria than in those not complicated by the elimination of the organism in the urine. In 9 positive cases Richardson found albumin to be present. In one there was a thick cloud, while in the remaining 8 there was a mere trace. Of 29 negative cases 15 showed albumin and on an average in greater quantity than in the positive cases. Casts were found in some of the positive and negative cases. In two cases described by Horton Smith, in which there were many bacilli, albumin was found to be absent, while the same phenomenon was described by Petruschky in one case. Out of 17 positive cases Horton Smith found that

albumin (which was apparently not explained by pyuria) was present in 7. Haematuria was got in one case, but this is a comparatively rare complication. Vincent states that albumin is not by any means a necessary concomitant of bacilli and this statement is borne out by my investigations. Of the 8 cases whose urines showed Eberth's bacillus, 4 had albuminuria. In 3 of these, however, its presence was probably due to the pus which was there and in none of them was there more than a cloudiness. In the 4th case albumin was got along with granular and hyaline casts but prior to the discovery of the organism. In one case (No. 10) where typhoid bacilli were not got, albumin was found and this again was probably due to the pus which was in small amount.

Pyuria

Pyuria existed in 3 of the 8 positive cases, but only to a small extent and discoverable by means of the microscope. There was no decided deposit in any case. In one other case pus was found and was due to the colon bacillus. In none of these cases did the patient complain of urinary trouble and there was no symptom of cystitis.

Blumer found this condition in 10 out of 60 cases examined by him while Horton Smith put the proportion as high as 50 per cent.

Gwyn found that 7 out of 8 cases with typhoid bacilluria suffered from pyuria and in 5 of

these there was decided cystitis.

That cystitis due to this bacillus is a rare condition is seen by the fact that out of 1200 cases Vincent found it to exist in only 2, and it is a complication but seldom seen in the Edinburgh Fever Hospital.

Turbidity.

In none of my cases was turbidity noticed. Petruschky describes it as occurring in only 3 out of 50 cases. Horton Smith in one series of observations gives it as happening in 2 out of 12 cases, while later he says he found it in 12 out of 14 urines examined and in which typhoid bacilli existed. Richardson draws attention to this as mentioned by Smith, but while in many cases he found the organism in great numbers, he does not state whether turbidity was present or not.

Severity.

In the 14 positive cases recorded by Richardson in his second series of observations 6 are put down as very severe clinically and 3 of these proved fatal. Seven are noted as severe or moderately severe and one as very mild. He says that "in a "general way the cases which showed typhoid bacilli in "the urine were of a more severe type as evidenced by "the clinical course and mortality. Especially to be

"noted is the tendency to relapse and complication."

Among the 23 positive cases, 4 had a relapse, and among the complications were 3 pneumonias, 1 cholecystitis, 1 phlebitis, 1 furunculosis and 1 epididymitis.

Of 29 negative cases, 1 proved fatal, 1 had a relapse and 1 suffered from phlebitis.

Of 17 cases in which Horton Smith had found bacilluria to exist 3 were fatal, 8 were noted as severe or very severe, 5 were moderately severe, and 1 was mild. Against these, of 28 negative cases, 4 were fatal, 6 very severe or severe, 4 moderately severe and 14 mild.

Five of the 8 cases which I examined and in which the specific germ was found were described as being very severe, 2 were noted as moderately severe while 1 was a mild case of enteric fever. Two cases suffered from a relapse (No. 5 and No. 7) and in one case (No. 8) phlebitis was got as a complication.

On the other hand only 2 of the 7 negative cases were very severe, 2 others were of moderate severity, while 3 were described as being of a mild type.

It thus seems fairly evident that the more severe the case the more chance there is of the urine being affected.

Table No. VI

Positive Cases

	Horton Smith	Dods Brown
Fatal	3	0
Very severe	4	5
Severe	4	
Moderately severe	5	2
Mild	1	1
	17	8

Negative Cases

Fatal	4	o
Very severe severe	6	2
Moderately severe	4	2
Mild	14	3
	28	7

Roseola.

The association of bacteriuria and rose spots was early commented on. Konjajeff held that bacteriuria indicated the presence of lymphoid nodules in the kidneys and these appeared at the same time as the typhoid spots. Neumann tried to make out that the two conditions always coincided, but many later writers do not favour this view. Richardson shows that 6 out of 9 positive cases presented them, while of 29 negative cases only 11 had the roseola. That there is more probability of bacilluria being got in those cases

with roseola than in those without this condition is seen by Table No. II. In each of the 8 cases in which typhoid bacilluria was present the spots were present, either well marked and typical or suspicious, whereas in the 7 without bacilluria only 3 had rose spots, the remaining 4 having none at all.

Summary.

To summarise what has been said, I think it is obvious that we have no means of accuracy by which we are enabled to say definitely that such and such a urine is infected with typhoid bacilli, other than by making a bacteriological examination.

That there is a possibility of its being infectious we can say when it is turbid, has an acid reaction and presents that peculiar shimmer, but on these alone we certainly cannot rely, because of the very large proportion of urines which contain the bacillus and in which these conditions do not exist.

Again because a patient has albuminuria or pyuria he does not necessarily have typhoid bacilluria, and the absence of the bacilli is not by any means proved if the urine is found free of these abnormal constituents. Many a clear non-albuminous urine is swarming with the bacillus, to discover which a bacteriological examination must be made.

IV

Pathology

The original hypothesis as to the Pathology of the condition was that the organism circulating in the blood irritated the kidney, and gave rise to a nephritis through which the passage of the bacillus from the blood into the urine was rendered possible. This theory breaks down at once in those cases in which there is an absence of albumin, and as shown by Melchior all the cases complicated by acute nephritis do not have typhoid bacilli in the urine. In 4 cases of enteric suffering from acute nephritis he found the organism in the urine of only one.

Another theory put forward is that bacilluria is due to a filtration of the bacilli from the blood, but on several occasions in which the urine was swarming with the organisms, the blood was examined and the bacillus was found only with great difficulty.

It is true that their presence may be due to suppuration in the kidney and to the passage of bacilli and pus into the urine, but that suppuration in the kidney is very rarely got is seen from the report of 289 post-mortem examinations of typhoid patients made at St. Bartholomew's Hospital. In only one case were renal abscesses found. Then again concomitant pyuria would of necessity be a constant but as we have seen this is not so.

Blumer's explanation is that the bacilli

pass from the rectum into the bladder through the tissues separating these two organs. It has been proved that if the rectum be irritated and cultures of certain bacteria be injected into it, a cystitis is very soon set up.

In typhoid fever it is exceptional to have a lesion as low down as the rectum and moreover it is known that although bacilluria is got well on in the disease it is only in the early stages that the bacillus can be found in the faeces.

The adequate explanation seems to be that one or two stray bacilli manage to pass through the kidney from the blood and get into the urine where they grow rapidly. This fluid has proved, experimentally, a very good medium for the growth of the bacillus typhosus, and in the bladder, where there is a suitable temperature and where the urine is regularly being renewed, everything is favourable for its further growth. This theory receives support from the fact that injections of disinfecting fluids, such as the perchloride of mercury, into the bladder cause the rapid and permament disappearance of the bacilli from the urine.

-V-

Treatment

It is only too obvious that typhoid bacilluria is a source of great danger not only to the patient, but to the general public. To overcome this risk, something must be done and some means must be taken to render the urine sterile. The drug which has proved of greatest value in this respect is undoubtedly urotropine. Richardson has made some interesting and useful researches with this drug and these go to show that it is a urinary disinfectant of the very highest value. In 9 cases the typhoid bacilli disappeared from the urine under its administration and in 8 of these this was brought about by 60 grains or less. One case required 200 grains to permamently remove the organism and in another case after 60 grains of urotropine had been given the urine was found free of the bacillus, yet 23 days later it was again found to be infected. The omission of the drug was followed on 3 separate occasions by the return of bacilluria, which complication was got rid of only after the fourth course.

Seven cases were followed for 7, 9, 13, 14, 17, 19, 43 and 66 days respectively, after the drug had been stopped and no bacilli were got in the urine. It seems fair to assume that the disappearence of the

specific germ in the last 3 or perhaps 4 cases was permament, but the same cannot be said about the others because I have found, as I shall detail below, the bacillus reappearing 11 and 12 days after the administration of the drug was stopped.

Another drug which Richardson made use of was salol. In one case he gave it in 10 grain doses t.i.d. for 14 days, with no benefit. In a second case its administration in similar doses for 10 days caused a disappearance of the organism. In a third case he failed with it, after which the patient was given urotropine and in two days the urine was clear.

Horton Smith found that 3o grains were sufficient in many cases to cause a disappearance of the bacilli, but as a routine practice he suggested it should be continued for several days because many cases require a much larger dose than 30 grains.

Another method of treatment used is irrigation of the bladder which Gwyn adopted in 5 of his cases. He used 1 in 50,000 perchloride of mercury and in a very short time the urine of 3 of these became normal.

In 2 other cases he used urotropine, to one of which, with nephritis and cystitis, he gave 10 grains t.i.d. and in two days no bacteria were seen on microscopic examination, but on making a culture from lc.c. he found ten colonies present. After five more

days no bacteria were got and the nephritis and cystitis cleared up.

In the 7th case, which was one of cystitis coming on in the third week of the disease, urotropine was given in 5 grain doses t.i.d. After 80 grains had been given no bacilli were found and the pyuria improved, but on the 11th day after 165 grains had been administered the bacilli and pus reappeared. The drug was continued for 6 days when the bacilli were again found to be absent.

Fuchs published in 1902 an account of the action of urotropine as a urinary antiseptic. The material for his investigation consisted of 41 cases of typhoid fever, 14 of whom had bacteria in the urine. The specific bacillus was found in only 4 of those and the bacillus coli communis and cocci were got in 6. The results which Fuchs obtained led him to the conclusion that urotropine had an inhibitory rather than an antiseptic action on typhoid bacilli. In 3 cases with typhoid bacilluria the number of organisms was markedly diminished on the second day while those urines with the colon bacillus were not appreciably affected.

Recently Dr. Gee and Dr. Andrews found that urotropine had a beneficial action on the urine of typhoid patients.

My own experience of urotropine leads me to think that the drug must be continued for a week or ten days in big doses in order to ensure the thorough disinfection of the urine and bladder

In case No. 5 urotropine was given on the 20th December in 7 grain doses t.i.d. On the 21st 10 grains t.i.d. were given and continued the following day. No typhoid bacilli were found on the 22nd, but an examination being made on the 2nd January the organism was found in great numbers. From the 2nd January the drug was administered in 15 grain doses 6 hourly up till the 7th January from which time the same dose was given 4 hourly and continued till the 9th January. The urine was found free of the organisms on the 9th and was so when examined again on the 17th January.

The second case in which urotropine was used was No. 6. The drug was commenced on the 12th December and given in 15 grain doses t.i.d. and so on the 13th. The urime was examined on the 13th when a few typhoid bacilli were found on cultivation along with bacillus coli communis. On the 14th December no typhoid bacillus was present or again on the 19th, but on the 24th December both bacillus typhosus and the colon bacillus were easily isolated from the urine. I was unable to follow this case further.

No. 7 was the third case treated

with urotropine. It was commenced on the 17th January in 15 grain doses every four hours and then for the next three days i.e. until the 20th inst, in the same amount but t.i.d. On the 17th, bacillus typhosus was present and also on the 19th, but on the 23rd, staphylococcus pyogenes aureus was the only organism cultivated.

In No. 5. 80 grains were sufficient to clear up the urine, but 12 days later it again became infected; while in No. 6 the urine became free of the bacillus after the patient had taken 90 grains, but in 11 days the organism was again found in large numbers. The 3rd case had as much as 225 grains of the drug before the urine was free of the organism.

In one case (No. 13) where only bacillus coli was in the urine urotropine was tried in gr.x doses every four hours. It was begun on the 12th December and continued till the 15th inst. On the 14th December the bacillus coli (and the bacillus pyocyaneus) was easily cultivated and again on the 17th and 27th. From this it appears as if this bacillus was not affected by the use of urotropine.

In case No. 1 another drug viz. acetozone was used. It was given to try its effect on the general condition and not specially because of the bacilluria, but in as much as it is lauded as of very great value in enteric fever, one was anxious to note

the result on the urinary condition. Twenty grains were taken and dissolved in one quart of distilled water, and 4oz. of this solution were given as a dose every four hours and continued for three weeks i.e. up till the 19th November. On two occasions on which the urine was examined during the time the patient was taking acetozone, the bacillus was found i.e. on the 7th and 16th November. On the 30th November eleven days after the drug was stopped the bacillus typhosus was again present in the urine in considerable numbers. My regret is that I was unable to try the drug in more cases but the results obtained in that one case seem to show that acetozone has little, if any action, as a urinary disinfectant.

From what has been said it is apparent that urotropine is the most useful drug which can be ordered in cases of typhoid bacilluria. It was introduced by Nicolaier as a urinary disinfectant and appears in the urine partly as urotropine and partly as formaldehyde. It is eliminated in about 15 minutes after administration and can be found for some days after it has been stopped. It has no prejudicial action on any abnormal renal condition.

Irrigation of the bladder with boracic solution is altogether useless, but a strong disinfectant such as perchloride of mercury of a strength of 1 in 50,000 even, is quite efficacious. This

method of treatment however is quite unnecessary when we have such a reliable and safe drug as urotropine.

VI

Public Health

I have shown above that the typhoid bacillus very soon disappears from the stools of the patients suffering from enteric and its place is taken by the colon bacillus, but although now the stools play little part in the spread of the disease, the patient really becomes more dangerous to those around and to the general public. The urine now may be teeming with the germ and the pollution of sheets and blankets is too easily caused and is extremely apt to be overlooked. How easy it is for one or two drops of the urine to infect the clothes and when we know that as many as 100,000,000 microbes may be got from one cubic centimetre, or roughly fifteen drops, it is easy to imagine how disastrous the results may be. Not only is this contamination liable to occur when the patient is in bed, but also during convalescence when the patient is going about and also after he is cured. How readily may the hands of a patient with typhoid bacilluria become infected by the urine and so give rise to trouble and be the source of further disease.

If proper precautions had been taken in the South African campaign how much disease and death might have been prevented, for, as Pratt Yule mentions, the urine and slops were oftentimes thrown on to the ground just outside the tents, regardless of their dangerous character. The result was that the bacilli were blown throughout the camp spreading disease everywhere. And what more natural thing can one imagine than a soldier, on the call of nature, going just outside a tent and micturating, and perhaps in close proximity to the water supply. In this way if typhoid bacilluria be present grave results might occur.

And what has been said about camps applies equally to other communities. From infected hands, clothes and food may be contaminated and the clothes are a source of danger not only to those in attendance or in the same house, but to those who have the washing of them.

One can readily understand precautions being taken with clothes which are stained with faeces, but those tainted with urine may be overlooked for a long time.

It is only necessary to mention how easily a water supply of a town, village or house may be unwittingly infected through the same cause.

VII

Conclusions

To overcome the danger of typhoid bacilluria it is not sufficient to give urotropine in small doses for a few days. It may perchance clear up the condition but the probability is that it will recur. As seen in two of my cases the typhoid bacilli disappeared under the administration of the drug after 80 grains and 90 grains respectively had been given, but in one case the organism reappeared in 12 days and in the other in 11 days after the drug had been stopped.

This may be explained by a stray bacillus finding its way through the kidney and growing in the bladder, or what seems more probable is that some bacilli had been lying dormant in the vesical wall and later took on active growth.

The conclusions which I think one is entitled to arrive at may be summarised as follows.

1. The bacillus typhosus exists in the urine of typhoid patients in from 30 to 35 per cent of cases.
2. In most cases they cause no symptoms and their presence is revealed only by a bacteriological examination.
3. Bacilluria is frequently accompanied by albuminuria and pyuria, but these are not necessary

concomitants.

4. The bacilli usually appear in the 3rd or 4th week of the disease and persist for a varying time - for weeks or months and even after the patient is cured.

5. Bacilluria is got more frequently in severe cases and in those with complications, but the severity of the case is not affected by the condition which is of no prognostic significance.

6. The presence of bacilli in the urine does not aid in the diagnosis except in some typhoid septicaemic cases.

7. The presence of the specific bacilli in the urine is more dangerous than their presence in the stools because (a) the disinfection of this fluid is apt to be neglected and all attention paid to the faeces which after the 3rd week may contain no typhoid bacilli. (b) Contamination of the urine is less apparent than that brought about by the faeces and thus clothes &c may be a source of great danger. (c) Pollution of a water supply is more likely to occur through urination than defaecation.

8. All typhoid patients at whatever stage of the disease should micturate into special receptacles where the urine should be disinfected. Urination during bathing and when outside should be strictly

forbidden.

9. All patients from the third week should be given urotropine in 10 grain doses t.i.d. for 10 days and after one week's interval administration of the drug should again be carried out for other 10 days. After this a bacteriological examination of the urine should be conducted,and if the bacillus be present the drug should be continued for a week after the urine is sterile.

Literature

Gwyn. John Hopk. Hosp. Bull. June 1899

Blumer John Hopk. Hosp. Reports No. V p. 327 1895

Karlinski Lancet 27th September 1890

Wright & Semple Lancet 27th July 1895

Horton Smith Lancet 2nd May 1899

" " Lancet 24th & 31st March & 14th April 1900

" " Brit. Med. Jour. 13th February 1897

" " Trans. Roy. Med. and Chir. Soc. 8th Feb. 1897

Corfield Lancet 22nd March 5th, 12th & 26th April and 3rd May 1902

Newman Brit. Med. Jour. 29th October 1898

Houston Brit. Med. Jour. 14th January 1899

Richardson Jour. of Exper. Med. May 1898

" " " " " January 1899

Vincent La Semaine Médicale p.85 1901

Lévi & Lemierre " " p.408 1901

Vincent " " p.88 1903

Munch " " p.121 1904

Besson Rev. de Med. June 1897

" " " " May 1898

Lewis Edin. Med. Jour. p.261 1901

Fuchs Brit. Med. Jour. 14th June 1902